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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/865,627	05/25/2001	M. Kathleen Kerr	9675-004	4100
20583	7590	12/24/2003	EXAMINER	
PENNIE AND EDMONDS 1155 AVENUE OF THE AMERICAS NEW YORK, NY 100362711			MORAN, MARJORIE A	
			ART UNIT	PAPER NUMBER
			1631	

DATE MAILED: 12/24/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/865,627

Applicant(s)

KERR ET AL.

Examiner

Marjorie A. Moran

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 22 September 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-34 is/are pending in the application.
- 4a) Of the above claim(s) 11, 12, 25 and 26 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-10, 13-24 and 27-34 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 25 May 2001 is/are: a) ☐ accepted or b) ☒ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 13) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.
a) ☐ The translation of the foreign language provisional application has been received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ 6) ☐ Other:

Election/Restrictions

Applicant's election with traverse of Group I, claims 1-10, 13-24 and 34 in a paper filed 9/22/03 is acknowledged. The traversal is on the ground(s) that the scope of claim 25 covers any interaction and is not limited to gene-non-gene interactions. This is not found persuasive because step (d) of claim 25 clearly recites a step of estimating "gene-non-gene interaction effects". In response to the request that examiner elucidate the "different modes of operation, different functions, or different effects" between the Groups, it is noted that the method of claim 25 (Group IV) recites steps of constructing data models and of transforming data not recited in claim 1 (Group I). A method reciting steps of constructing models necessarily requires a different "function" than does a method which does not construct models. The transformation of data will inherently change the operators of the dataset used in claim 25 and thus requires use of a different product (i.e. dataset) than is recited in claim 1, and will necessarily result in a different outcome (effect) than will the method of claim 1, which does not recite a step of transforming data. In response to the argument that a search for all Groups would not require separate or burdensome searches, the examiner maintains that as the method(s) of each Group recites different limitations/steps, a search for any one Group is not necessarily a search for any other Group. In addition, a search for any single Group requires a search of nonpatent literature and foreign patents, as well as US patents. For these reasons, the examiner maintains that the restriction is proper and that a search for more than a single Group would be burdensome.

Claims 27-33 have been amended to depend from elected claims and are therefore also considered elected.

Applicant's arguments with regard to the election of species requirement are persuasive, therefore the election of species requirement is withdrawn.

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The restriction requirement is still deemed proper and is therefore made FINAL.

Claims 11-12 and 25-26 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected method, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in a paper filed 9/22/03.

An action on the merits of elected claims 1-10, 13-24 and 27-34 follows.

Drawings

The informal drawings are not of sufficient quality to permit examination. Accordingly, new drawings are required in reply to this Office action.

Applicant is given a THREE MONTH time period to submit new drawings in compliance with 37 CFR 1.81, said time period for response to run concurrently with the time period for response to this Office Action. Extensions of time may be obtained under the provisions of 37 CFR 1.136(a). Failure to timely submit new drawings will result in **ABANDONMENT** of the application.

Information Disclosure Statement

The IDS filed 8/24/01 has been considered in full.

Specification

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. See e.g. pages 3-4. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

Claim Objections

Claims 2, 3, 5-7, 14-15, and 17-19 are objected to because of the following informalities: For clarity, the term --and-- should be inserted before "the step" in line 2 of each of claims 2, 3, 14, and 15. In line 1 of each of claims 5-7 and 17-19, the term "factors" should be --factor--. Appropriate correction is required.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-10, 13-24 and 27-34 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

The method of claims 1-10, 23, and 27-33 is merely a mathematical manipulation of data. The apparent series of mathematical steps for the data manipulation is equivalent to a mental process. Applicant is reminded that mental processes are not statutory subject matter under 35 USC 101.

The claimed subject matter is not restricted to be a computer-implemented method, however the specification indicates that the disclosed process is a program and thus is one which may be performed on a computer. In the event that the claimed method steps are implemented by a computer, the method steps are not statutory as any computer implemented method must produce a result which is concrete, tangible, and useful (MPEP 2106.IV.B). The claimed method is directed to a method of estimating the effects of factors and interactions between factors in a gene microarray experiment, but does not identify the "effects" to be estimated, or what is affected. Nor are any elements of the gene microarray identified in the claims. If an "effect" were upregulation, inhibition, etc., then estimating the "effect" of factors and interactions (gene expression levels? correlation to a known disease or disorder?) on an array of genes such that expression of a sequence is positively correlated with a known disease or disorder, then the correlation (result) MAY be considered a concrete, tangible and useful one.

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No correlation to a known disease or disorder is recited in the claims. The specification discloses, on page 8, that the goal of many (microarray) experiments is to determine the effect of one or more independent variables on one or more dependent variables. As set forth above, the instant claims do not recite what the "effect" itself is, or what it is intended to act upon. The claims do not recite dependent or independent variables. As claims recite only mathematical manipulation of data, and do not recite a concrete, tangible and useful result, the claims are not statutory.

Claims 13-22 and 24 are directed to a system with a processor and memory to run a program similar to the method of claim 1. Claims 13-22 do not recite any structural limitations.

"The mere fact that a hardware element is recited in a claim does not necessarily limit the claim to a specific machine or manufacture." See also *In re Iwahashi*, 888.F.2d 1370, 1374-75, 12 USPQ 2d 1908, 1911-12 (Fed. Cir. 1989), recited with approval in *Alappat*, 33 F.3d at 1544 n.24, 31 USPQ2d at 1558.

It is noted that a claim may be statutory when it identifies the physical structure of an item of manufacture in terms of its hardware, or a hardware and software combination. Claims 13-22 do not recite any physical or hardware limitations, as set forth above. It is also noted that a claim to a product which has a practical application in the arts may be statutory; e.g. a computer comprising a program which produces a concrete, tangible, and useful result, as decided in *Alappat* (312 USPQ2d 1557) and *State Street* (47 USPQ2d 1601). As set forth above, the claimed method does not produce a concrete, tangible, and useful result, therefore the computer readable medium comprising a program for running such a method would not have a practical application in the arts, and is not statutory.

Claim 34 is directed to a computer readable medium comprising instructions for performing the method of claim 1. It is noted that a claim to a product which has a practical application in the arts may be statutory; e.g. a computer comprising a program which produces a concrete, tangible, and useful result, as decided in *Alappat* (312 USPQ2d 1557) and *State Street* (47 USPQ2d 1601). As set forth above, the claimed method does not produce a concrete, tangible, and useful result, therefore the computer readable medium comprising a program for running such a method would not have a practical application in the arts, and is not statutory.

Claims 1-10, 13-24 and 27-34 are rejected under 35 U.S.C. 101 because the claimed invention lacks patentable utility.

As set forth above, the claims are directed to a method, system, and medium comprising a program for running the method, for estimating the effects of factors and interactions between factors in a gene microarray experiment, but do not identify the "effects" to be estimated, nor what is affected. No elements of the gene microarray (from which the effects are estimated?) are identified in the claims. If an "effect" were upregulation, inhibition, etc., then estimating the "effect" of factors and interactions (gene expression levels? correlation to a known disease or disorder?) on an array of genes such that expression of a sequence is positively correlated with a known disease or disorder, then the correlation (result) MAY be a useful one. No correlation to a known disease or disorder is recited in the claims. The specification discloses, on page 8, that the goal of many (microarray) experiments is to determine the effect of one or more independent variables on one or more dependent variables. As set forth above, the instant claims do not recite what the "effect" itself is, or what it is intended to act upon. The claims do not recite dependent or independent variables. A claim which merely recites estimating the effects of an independent variable on a dependent variable, where the variables are not identified, would not have a utility as further research would be required to determine what the effect IS. As set forth in MPEP 2107, a "use" to do further research is not a utility under 35 USC 101. As applicant has failed to disclose enough information about the invention to make its usefulness *immediately apparent* to those familiar with the technological field of the invention, the claims lack utility. See MPEP 2107.01, and the analyses of utility in *Brenner v. Manson*, 383 U.S. 519, 148 USPQ 689 (1966) and *In re Ziegler*, 992 F.2d 1197, 26 USPQ2d 1600 (Fed. Cir. 1993).

Claim Rejections - 35 USC § 112-1

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-10, 13-24 and 27-34 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. This is a LACK OF ENABLEMENT rejection.

The factors to be considered in determining what constitutes undue experimentation were affirmed by the court in *In re Wands* (8 USPQ2d 1400 (CAFC 1986)). These factors are the quantity of experimentation; the amount of direction or guidance presented in the specification; the presence or absence of working examples; the nature of the invention; the state of the prior art; the level of skill of those in the art; predictability or unpredictability of the art; and the breadth of the claims.

The claims are not enabled because neither the instant specification nor the prior art teach how to determine effects of factors and interactions on an unknown entity. The claims are directed to a method, and a system and medium for running the method, of estimating the effects of factors and interactions of factors in a gene expression microarray experiment, but do not identify what the effects themselves are nor what the effects are to be directed toward or what the effects are to act on (i.e. the claims do not recite WHAT is affected).

The specification provides guidance on page 8 that the goal of "many experiments" is to determine the effect of an independent variable on a dependent variable. The claims do not recite dependent or independent variables, thus it does not seem that the disclosure of page 8 is directed to the claimed method. The specification provides guidance on pages 8-11, in what appears to be a prophetic example, that the effect of defined factors on luminescence may be

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estimated *when the same set of genes* is present on every array in an experiment. The specification discloses on page 11 that a separation of "global" versus "non-gene" effects is critical to the invention. These limitations do not appear to be reflected in the claims, nor are the various steps disclosed on pages 8-11 (linear regression, inversion of a matrix, etc.) recited in the instant claims.

The state of the prior art is such that a method of analysis of variance for gene expression microarray data, similar to that disclosed, is known (See KERR et al. IDS ref: J. Comp. Biol. (2000) vol. 7, pages 819-837). However, the method of prior art also requires that "effects" be identified (e.g. dye effects or variety effects) in order to be calculated/estimated (see e.g. pages 9-10). Neither the instant specification nor the prior art provide guidance on how to estimate unknown effects or known effects on an unknown recipient. As taught by KERR et al. (*supra*), as more variables are added to a model, the degrees of freedom expand until it becomes difficult to predict the effects for all variables. Therefore, unless variables are explicitly identified and a decision made to include or exclude particular combinations of variables (i.e. interactions between SPECIFIC variables), effects can not be estimated (i.e. effects are completely confounded). Thus, there appears to be a high degree of uncertainty in the art for estimating effects where the effects and/or variables are not identified.

The degree of skill in the statistical art is acknowledged to be high. Despite the high level of skill in the art, it would require undue experimentation for one of skill in the art to perform the claimed method due to the lack of guidance in either the specification or prior art to perform a method of estimating effects wherein the "effects" and/or variables to be affected are unknown.

Claim Rejections - 35 USC § 112-2

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-10, 13-24, and 27-34 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1 and 13 recite a method and system for estimating "the effects" of factor and interactions of factors. Those skilled in the art generally estimate or determine an effect OF something ON something else. It is unclear what applicant intends to estimate an effect ON, therefore the claims are indefinite.

Claims 1 and 13 recite a method for estimating effects in a gene expression microarray experiment "generating a microarray dataset". It is unclear if applicant merely intends to recite an intended use for the gene expression microarray of lines 2-3 of each claim, or intends to recite a method of generating a microarray dataset, or intends some other limitation. If applicant intends to recite an intended use, then it is noted that the "use" does not structurally limit the microarray dataset. If applicant intends to limit the method/program to one wherein a microarray dataset is generated, then this limitation should be recited as positive, active method steps. Applicant is reminded that such steps must be fully supported and enabled by the specification.

Claims 2, 3, 14, and 15 limit a factor to be "characterized by" a level or number of levels. It is unclear if applicant intends the factors to comprise a level or number of levels, to be identified by a level or number of levels, to be associated with a level or number of levels, etc. Use of the term "characterized by" renders the limitation intended for a factor unclear, therefore the claims are indefinite.

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Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marjorie A. Moran whose telephone number is (703) 305-2363 until January 12, 2004. After that date, the telephone number will be (571)272-0720. The examiner can normally be reached on Monday to Wednesday, 7:30 am to 4 pm EST, Thursday, 7:30 am to 6 pm EST, and Friday, 7 am to 1:30 pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward can be reached on (703) 308-4028. After January 12, 2004, Michael Woodward can be reached at (571) 272-0722. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 305-3524.

MARJORIE MORAN
PATENT EXAMINER

Marjorie A. Moran

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